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USE OF LIPID CONJUGATES IN THE TREATMENT OF DISEASE

This appln claims benefit of 60/174,907 01/10/00 and 60/174,905 01/10/00

FIELD OF THE INVENTION

- 5 The present invention provides administering a class of pharmaceutically active lipid conjugate compounds directed to treating disease, including obstructive respiratory disease, colitis, Crohn's disease, central nervous system insult, multiple sclerosis, contact dermatitis, psoriasis, cardiovascular disease, including prophylaxis for invasive procedures, invasive cellular
- 10 proliferative disorders, anti-oxidant therapy, hemolytic syndromes, sepsis, acute respiratory distress syndrome, tissue transplant rejection syndromes, autoimmune disease, viral infection, chlamydia infection, and hypersensitivity conjunctivitis.

BACKGROUND OF THE INVENTION

- 15 Some high molecular weight conjugates have been described in US 5,064,817, and in the publications referenced herein, in particular wherein the conjugated moiety is dodecandioic, dextrane, dextranamide, carboxymethylcellulose, carboxymethylcellulose-acyl, poly-D-glutamic acid,
- 20 polyacrylic acid, polyethylene glycol, hydroxyethyl starch, heparin, hyaluronic acid, and polygleatin ('hemacell'), but these compounds were not known to be of wide-spectrum pharmacological effectiveness. These compounds are known to have the pharmacological activity of inhibiting the enzyme phospholipase A₂ (PLA₂, EC 3.1.1.4), which catalyzes the breakdown of
- 25 phospholipids at the sn-2 position to produce a fatty acid and a lysophospholipid. The activity of this enzyme has been correlated with various cell functions, particularly with secretory processes such as exocytosis and eicosanoid production (prostaglandins, thromboxanes and leukotrienes). The biological activity ascribed to these mostly phospholipid
- 30 derivatives was limited to inhibition of platelet aggregation, thromboxane secretion, and selective inhibition of phospholipase A₂. Accordingly, the use of PLA₂-inhibitors was proposed for treatment of diseases which are associated with enhanced cellular secretions, such as in allergy and